

2832

PCT/US99/28282

## PATENT COOPERATION TREATY

09/600346

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents  
United States Patent and Trademark  
Office  
Box PCT  
Washington, D.C.20231  
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year)

25 October 2000 (25.10.00)

International application No.

PCT/US99/28282

Applicant's or agent's file reference

18564-24-1PC

International filing date (day/month/year)

30 November 1999 (30.11.99)

Priority date (day/month/year)

01 December 1998 (01.12.98)

Applicant

SUNSHINE, Steven, A. et al

1. The designated Office is hereby notified of its election made:



in the demand filed with the International Preliminary Examining Authority on:

28 June 2000 (28.06.00)



in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

TO 2800 MAIL ROOM  
9-10-00  
10/10/00

The International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

R. Forax

Telephone No.: (41-22) 338.83.38

2832

09600346

15

## PATENT COOPERATION TREATY

## PCT

REC'D 28 NOV 2000

WIPO PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 18564-24-IPC	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US99/28282	International filing date (day/month/year) 30 NOVEMBER 1999	Priority date (day/month/year) 01 DECEMBER 1998
International Patent Classification (IPC) or national classification and IPC Please See Supplemental Sheet.		
Applicant CYRANO SCIENCES, INC.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.	
2. This REPORT consists of a total of <u>4</u> sheets. <input type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT). These annexes consist of a total of <u>0</u> sheets.	
3. This report contains indications relating to the following items:  I <input checked="" type="checkbox"/> Basis of the report II <input type="checkbox"/> Priority III <input type="checkbox"/> Non-establishment of report with regard to novelty, inventive step or industrial applicability IV <input type="checkbox"/> Lack of unity of invention V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement VI <input type="checkbox"/> Certain documents cited VII <input type="checkbox"/> Certain defects in the international application VIII <input type="checkbox"/> Certain observations on the international application	

RECEIVED  
FEB - 6 2001  
TECHNOLOGY CENTER 2800

Date of submission of the demand 28 JUNE 2000	Date of completion of this report 02 NOVEMBER 2000
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer HEZRON E. WILLIAMS Telephone No. (703) 305-4705 <i>Hezron E. Williams</i>

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/28282

**I. Basis of the report****1. With regard to the elements of the international application:\***

- ☒ the international application as originally filed  
the description:  
pages 1-18 , as originally filed  
pages NONE , filed with the demand  
pages NONE , filed with the letter of \_\_\_\_\_
- ☒ the claims:  
pages 19-23 , as originally filed  
pages NONE , as amended (together with any statement) under Article 19  
pages NONE , filed with the demand  
pages NONE , filed with the letter of \_\_\_\_\_
- ☒ the drawings:  
pages 1-3 , as originally filed  
pages NONE , filed with the demand  
pages NONE , filed with the letter of \_\_\_\_\_
- ☒ the sequence listing part of the description:  
pages NONE , as originally filed  
pages NONE , filed with the demand  
pages NONE , filed with the letter of \_\_\_\_\_

**2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.**

These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

**3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:**

- ☐ contained in the international application in printed form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

**4. ☒ The amendments have resulted in the cancellation of:**

- ☒ the description, pages NONE
- ☒ the claims, Nos. NONE
- ☒ the drawings, sheets/fig NONE

**5. ☐ This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\***

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

\*\*Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/28282

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. statement**

Novelty (N)	Claims <u>1-28</u>	YES
	Claims <u>NONE</u>	NO
Inventive Step (IS)	Claims <u>1-28</u>	YES
	Claims <u>NONE</u>	NO
Industrial Applicability (IA)	Claims <u>1-28</u>	YES
	Claims <u>NONE</u>	NO

**2. citations and explanations (Rule 70.7)**

Claims 1-28 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest a device, system or method for detecting analytes in a fluid via a sensor array of two or more sensors connected electrically to an electrical measuring apparatus, where one sensor is designed such that it comprises a region of aligned electrically conductive material (the other sensor(s) being designed such that they comprise other region(s) of non-specified material in terms of being electrically non-aligned and/or nonconductive). Prior arts Simendinger III et al. (5,742,223) and/or Jin et al. (4,644,101) reveal a material design that is compatible with the instant invention but neither teaches, suggests the application of such material design towards sensing analytes or any other chemical substances in a fluid or in any other environment; while Lewis et al. (5,571,401) reveals an electrical resistor type of chemical sensor for detecting fluid borne analytes via use of a plurality of non-aligned material regions connected between two electrical leads: which references either applied solely or in combination do not teach the aligned conductive material region type of sensor array used for chemical detection of analytes in a mixture medium. Accordingly, the testing device, system and method is deemed to contain novelty, to constitute an inventive step (or steps), and to manifest a high degree of industrial applicability from the vantage point of one possessing ordinary skill in the art at the time of the invention, even for a skilled laboratory artisan or fluid sensor designer who was privy to wide ranges of all known analogous prior art during that time period.

----- NEW CITATIONS -----  
NONE

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/28282

**Supplemental Box**

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

**CLASSIFICATION:**

The International Patent Classification (IPC) and/or the National classification are as listed below:

IPC(7): G01N 27/26, 27/12, 27/22; G08B 17/10; G01R 27/26; H01C 7/10 and US Cl.: 73/31.05, 23.32; 324/71.1; 340/632; 338/21; 422/98, 90, 83, 68.1, 82.02; 205/787, 775, 782.5; 204/418, 415, 406; 436/150

CORRECTED VERSION

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
8 June 2000 (08.06.2000)

PCT

(10) International Publication Number  
WO 00/33062 A1

(51) International Patent Classification: G01N 27/26,  
27/12, 27/22, G08B 17/10, G01R 27/26, H01C 7/10

(21) International Application Number: PCT/US99/28282

(22) International Filing Date:  
30 November 1999 (30.11.1999)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
09/201,999 1 December 1998 (01.12.1998) US

DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,  
IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,  
LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT,  
RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA,  
UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM,  
KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent  
(AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent  
(AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU,  
MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM,  
GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:  
— With international search report.

(71) Applicant (for all designated States except US):  
CYRANO SCIENCES, INC. [US/US]; 73 North  
Vinedo Avenue, Pasadena, CA 91107 (US).

(88) Date of publication of the revised international search  
report: 21 September 2000

(72) Inventors; and

(75) Inventors/Applicants (for US only): SUNSHINE,  
Steven, A. [US/US]; 985 S. Oakland Avenue, Pasadena,  
CA 91106 (US). MUNOZ, Beth, C. [US/US]; 451 S.  
Oakland Avenue, Pasadena, CA 91107 (US).

(48) Date of publication of this corrected version:  
7 December 2000

(74) Agents: SNYDER, Joseph R. et al.; Townsend and  
Townsend and Crew LLP, 8th Floor, Two Embarcadero  
Center, San Francisco, CA 94111 (US).

(15) Information about Corrections:  
see PCT Gazette No. 49/2000 of 7 December 2000, Section  
II  
Previous Correction:  
see PCT Gazette No. 38/2000 of 21 September 2000, Sec-  
tion II

(81) Designated States (national): AE, AL, AM, AT, AU, AZ,  
BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK,

For two-letter codes and other abbreviations, refer to the "Guid-  
ance Notes on Codes and Abbreviations" appearing at the begin-  
ning of each regular issue of the PCT Gazette.

(54) Title: ALIGNED PARTICLE BASED SENSOR ELEMENTS

(57) Abstract: The present invention relates to a sensor array for detecting an analyte in a fluid, comprising first and second sensors formed by chemically sensitive resistors, wherein the first sensor comprises a region of aligned conductive material; or where each of the sensors comprises alternating regions of nonconductive regions and aligned conductive regions with each resistor providing an electrical path through both the nonconductive region and the aligned conductive region, while each sensor manifests a different electrical resistance during contact with sample fluids having different analyte concentrations via the monitoring arrangement of having the sensors electrically connected to an electrical measuring apparatus. The aligned conductive particle material is aligned by exposure to either of an electric, magnetic, optical, photo-electric, electromagnetic or mechanical field, which serves to improve signal to noise ratio of vapor sensors allowing Lower Detection Limits for vapors being sensed. Such Lower Detection Limits allow for identification of lower concentrations of hazardous material and is advantageous in medical applications, such as detection of disease states in a patient.

RECEIVED  
JAN 16 2001  
BIOLOGY CENTER 2800

WO 00/33062 A1

## ALIGNED PARTICLE BASED SENSOR ELEMENTS

5

### CROSS-REFERENCE TO RELATED APPLICATIONS

This application claims priority to U.S. Patent Application Serial Number 09/201,999, filed December 1, 1998, the disclosure of which is hereby incorporated by reference in its entirety for all purposes.

10

### BACKGROUND OF THE INVENTION

Electronic noses are artificial sensory systems that are able to mimic chemical sensing. In some instances, electronic noses are arrays of sensors, which are able to generate electrical signals in response to analytes or vapors. For instance, it is possible to detect volatile materials by directly or indirectly measuring a response, such as a resistance, across each of the sensors in the array. Moreover, by providing different variables in each sensor of the array, such as the polymeric make-up of the sensors, it is possible to characterize various chemical materials according to the response of the array to that volatile material.

The potential applications of electronic noses are great. Examples of applications include, but are not limited to, environmental control, quality control, assessment of food and beverage products. For example, in relation to fish freshness, long chain carbonyl compounds, such as myristaldehyde, can be correlated with fresh fish, whereas short chain alcohols, dimethylsulfide and amines, which increase as a function of time, are characteristic of foul smelling fish.

U.S. Patent No. 5,571,401, which issued to Lewis *et al.* (incorporated herein by reference), discloses sensor arrays useful for the detection of analytes. Each of these sensors comprise a resistor having a plurality of alternating nonconductive regions and conductive regions. As explained therein, gaps exist between the conductive regions and the nonconductive regions. In these sensors, the electrical path length and resistance of a given gap are not constant, but change as the nonconductive region absorbs, adsorbs or imbibes an analyte. The dynamic aggregate resistance provided by these gaps is, in part, a function of analyte permeation of the nonconductive regions.

The foregoing sensor is based on a conductive network in a nonconductive matrix. The swelling of the nonconductive matrix causes the conductive region to move apart changing the resistance of the sensor. The change in the resistance of the sensor can be correlated to the concentration of the vapor to be detected. The greater the resistance change for a given level of vapor, the lower the detection limit of the vapor being identified. It is thus advantageous to maximize the resistance change associated with the sensor elements.

One of the major challenges in sensor technology today is to enhance the signal-to-noise ratio (S/N) of a sensor element. By increasing the S/N of a sensor element, a lower detection limit is possible (*i.e.*, the lower the concentration of analyte it is possible to detect). This is particularly useful in applications such as the detection of low concentrations of explosives, landmine detection or in medical applications such as in the detection of microorganism off-gases.

The response of the sensors upon exposure to vapor is dependent on various factors. One such factor is the percentage of connected paths that are broken. The number of connected paths prior to exposure to a vapor is related to the percolation threshold. The percolation threshold is defined as the particle volume fraction at which the conductivity of the resistor increases rapidly (*i.e.*, an infinite number of conductive paths are formed and the lattice essentially transforms from an insulator to a conductor). At low volume loadings, there are few connected paths; whereas at high volume loadings there are many connected paths. However, at low volume loadings, there is greater sensor resistance. Unfortunately, there is concomitantly a high degree of noise at low volume loadings so that the signal to noise ratio is unsatisfactorily low.

In view of the foregoing, there is a need in the art to improve the signal to noise of vapor sensors while maintaining low volume loading. Low volume loading sensors result in more resistance and thereby a broader detection limit and greater dynamic range. The current invention fulfills this and other needs.

### SUMMARY OF THE INVENTION

In certain aspects, the present invention provides a sensor array for detecting an analyte in a fluid, comprising: first and second sensors wherein the first sensor comprises a region of aligned conductive material; and wherein the sensor array is electrically connected to an electrical measuring apparatus. Preferably, the first and



second sensors are first and second chemically sensitive resistors, each of the chemically sensitive resistors comprising: a plurality of alternating regions comprising a nonconductive region, such as an organic material, and an aligned conductive region. The aligned conductive region comprises an aligned conductive material compositionally different from the nonconductive region. Moreover, each sensor, such as a resistor, provides an electrical path through the nonconductive region and the aligned conductive region; and a first response such as an electrical resistance, when contacted with a first fluid comprising an analyte at a first concentration, and a second response when contacted with a second fluid comprising the analyte at a second different concentration.

In certain embodiments, the conductive region can be aligned using various processing techniques including, but are not limited to, exposure to an electric field, a thermal field, a magnetic field, an electromagnetic field, a photoelectric field, a light field, a mechanical field or combinations thereof.

Various materials can form the aligned conductive region of the present invention. Such materials include, but are not limited to, conductive materials, semi-conductive materials, magnetic materials, photoresponsive materials and combinations thereof. The aligned conductive materials are preferably embedded in an organic matrix, such as a polymeric matrix.

In another aspect, the present invention relates to a system for detecting an analyte in a fluid, the system comprising: a sensor array comprising first and second sensors wherein the first sensor comprises a region of aligned conducting material. Preferably, the first and second sensors are first and second chemically sensitive resistors, each chemically sensitive resistor comprising a plurality of alternating regions comprising a nonconductive region and an aligned conductive region. Preferably, the aligned conductive region comprises an aligned conductive material compositionally different than the nonconductive region. Each sensor, such as a resistor, provides an electrical path through the nonconducting region and the aligned conductive region, a first response such as an electrical resistance, when contacted with a first fluid comprising an analyte at a first concentration and a second different response when contacted with a second fluid comprising the analyte at a second different concentration, wherein the difference between the first response and the second response of the first chemically sensitive resistor being different from the difference between the first response and the second response of the second chemically sensitive resistor under the same conditions; an

electrical measuring device electrically connected to the sensor array; and a computer comprising a resident algorithm; wherein the electrical measuring device detecting the first and the second responses in each of the chemically sensitive resistors and the computer assembling the responses into a sensor array response profile.

5           In yet another aspect, the present invention relates to a method for detecting the presence of an analyte in a fluid that can be either a liquid or a gas. The method comprising: providing a sensor array comprising first and second sensors, wherein the first sensor comprises a region of aligned conductive material; and contacting the sensor array with the analyte to produce a response thereby detecting the presence of  
10 the analyte. Preferably, the first and second sensors are first and second chemically sensitive resistors, each comprising a plurality of alternating regions comprising a nonconductive region, such as an organic material, and an aligned conductive region. The aligned conductive region comprises an aligned conductive material compositionally different from the nonconductive region. In this method, each resistor provides an  
15 electrical path through the nonconducting region and the aligned conductive region, a first response such as an electrical resistance, when contacted with a first fluid comprising an analyte at a first concentration and a second different response when contacted with a second fluid comprising the analyte at a second different concentration.

          These and other features and advantages of the invention will be more  
20 readily apparent and understood when read with the detailed description that follows.

### BRIEF DESCRIPTION OF THE DRAWINGS

          Figure 1 shows a graph of a typical resistance versus volume loading for a non-aligned composite sensor.

25           Figure 2 shows a graph of resistance versus volume loading for a composite sensor where the particles have been aligned.

          Figure 3 shows optical micrographs of unaligned sensor (left) and aligned sensor (right) Black Pearl 2000 (40 wt %) in 1,2-polybutadiene.

## DETAILED DESCRIPTION OF THE INVENTION AND PREFERRED EMBODIMENTS

Improvement of the signal to noise ratio of vapor sensors allows for lower  
5 detection limits by increasing the dynamic range. Lower detection limits allow for the  
identification of lower concentration of materials. This is particularly useful when  
detecting hazardous materials or in various medical applications. Surprisingly, it has now  
been discovered that by intentionally aligning the conductive region, there is an increase  
in the detection limit, *i.e.*, the sensor is capable of detecting lower concentrations of  
10 analyte. As such, the present invention provides a sensor array for detecting an analyte in  
a fluid, comprising: first and second sensors wherein the first sensor comprises a region  
of aligned conducting material; and wherein the sensor array is connected to an electrical  
measuring apparatus. Preferably, the first and second sensors are first and second  
chemically sensitive resistors, each of the chemically sensitive resistors comprising: a  
15 plurality of alternating regions comprising a nonconductive region, such as a  
nonconductive organic material, and aligned conductive region, such as an aligned  
conductive material or particle. The aligned conductive region is compositionally  
different from the nonconductive region. The sensors such as resistors, provide an  
electrical path through the alternating regions comprising a nonconductive region, such as  
20 an organic material, and an aligned conductive region, a first response when contacted  
with a first fluid comprising an analyte at a first concentration, and a second response  
when contacted with a second fluid comprising the analyte at a second different  
concentration.

As explained previously, the response upon exposure to a vapor is  
25 dependent on various factors. One such factor is the percentage of connected paths in the  
alternating regions that are broken. The number of connected paths prior to exposure to a  
vapor is related to the percolation threshold. The percolation threshold is defined as the  
volume fraction at which the conductivity of the resistor increases rapidly. At low  
volume loadings, there are very few connected paths. At high volume loadings, there are  
30 many connected paths. Upon exposure to vapors, composite sensors will exhibit a large  
change in resistance near their percolation threshold. Before the advent of the present  
invention, the noise level associated with such low volume loadings was prohibitively  
high. However, by aligning the conductive region, lower volume loadings can now be

used. Moreover, by aligning the conductive region, the percolation threshold is easier to obtain at low volume loadings.

The sensors of the present invention have an aligned conductive region that results in reduced percolation thresholds. Reduced percolation thresholds mean that a slight swelling of the composite sensor can result in a very large change in resistance. This is because the few conductive particles are all participating in the connected paths, and any discontinuity in the connectivity results in a large resistance change. Thus, the alignment of the conductive region results in all of the particles participating in the connected electrical paths. By aligning the conductive region, these systems will produce a stable base resistance and thereby enhance the signal-to-noise ratio. To achieve equivalent or near equivalent noise levels, it is important to ensure that the alternating regions are stable. This can be accomplished in the present invention by, for example, cross-linking the polymer matrix in the nonconducting region or by any other suitable means.

The alignment of the conductive region, *e.g.*, material or particles, is effected through the application of various processing techniques. For instance, polarization techniques can be used to align the conducting region. Suitable polarization techniques include, but are not limited to, exposure to an electric field, a thermal field, a magnetic field, an electromagnetic field, a photoelectric field, a light field, a mechanical field or combinations thereof. The techniques employed to align the particles depends in part on the particle composition.

Suitable particles for use in the present invention include particles with a permanent magnetic dipole including, but not limited to, iron, nickel or cobalt require the use of a magnetic field for polarization to occur. Particles such as carbon black, coke, C<sub>60</sub>, and the like, TiO<sub>2</sub>, BaTiO<sub>3</sub>, In<sub>2</sub>O<sub>3</sub>, SnO<sub>2</sub>, Na<sub>x</sub>Pt<sub>3</sub>O<sub>4</sub>, conducting polymers, metals such as platinum, copper, gold, silver *etc.*, polarize with application of an electric field. In some embodiments, the conductive material is a conducting polymer, or an insulating polymer with conductive fillers. Suitable conductive polymers are disclosed in U.S. Patent No. 5,571,401, which issued November 5, 1996, and WO 99/31494, which published on June 24, 1999. As disclosed in WO 99/31494, the sensors taught therein comprise substituted polythiophenes. One polymer is poly (3,3''-dihexyl-2-2':5',2''-terthiophene). In a preferred embodiment, the conductive particle is carbon black.

In an equally preferred embodiment, the conductive material can be a particle, such as a gold nanoparticle, with a capping ligand shell. A preferred nanoparticle is disclosed in WO 99/27357, entitled "Materials, Method and Apparatus for Detection and Monitoring Chemical Species," published June 3, 1999. Examples of colloidal nanoparticles for use in accordance with the present invention are described in the literature (see, Templeton *et al.* *J. Am. Chem. Soc.* (1998) **120** :1906-1911; Lee *et al.*, *Isr. J. Chem.* (1997) **37** :213-223 (1997); Hostetler *et al.* *LANGMUIR* (1998) **14** :17-30; Ingram *et al.*, *J. Am. Chem. Soc.*, (1997) **119** :9175-9178; Hostetler *et al.*, *J. Am. Chem. Soc.* (1996) **118** :4212-4213; Henglein *J. Phys. Chem.* (1993) **97** :5457-5471; Zeiri, *J. Phys. Chem.* (1992) **96** :5908-5917; Leff *et al.*, *LANGMUIR* (1996) 4723-4730. Moreover, particles such as copper phthalocyanine and phenothiazine polarize when illuminated. All of these polarization techniques can be used to generate sensors of the present invention.

Polarization processing, such as magnetic field processing, involves exposure to various polarization mechanisms having different directions and optionally, different strengths. For example, during fabrication of the present sensors, exposure to a magnetic field can optionally be in one direction, such as in the x-, y- or z-direction; in two directions, such as x- and y-directions, x-and z-directions or y- and z-directions; or in three directions, such as x-, y- and z-directions. In a preferred embodiment, the polarization processing is along the same axis as the vapor measurement. For instance, if the vapor measurement is along the z-direction, particle alignment will be along the z-direction. In an equally preferred embodiment, the direction of expansion of the alternating regions is along the same axis as the vapor measurement. As used herein, the x-, y-, and z-axes have their traditional meaning, *i.e.*, the x and y axes are in the plane of the sensor substrate and the z axis is perpendicular to the x and y origins.

In addition to magnetic field processing, sensor fabrication of the present invention can include other modes of polarization. For example, photosensitive conductive material will be exposed to optical radiation, such as visible, infrared or ultraviolet light. Electrosensitive conductive material involves exposure to electric fields having different directions and different strengths.

As previously discussed, enhancing the response of the sensor can be accomplished by confining the direction of expansion of the alternating regions to be along the axis of measurement or, preferably, along the axis of the particle alignment.

For instance, a polymer can have a 2% volume expansion on exposure to a certain vapor concentration. If this swelling can be isolated to one dimension, then the linear expansion can be as high as 8% causing a much larger change in resistance than would occur without confinement.

5                   Aligning the conductive region *e.g.*, material or particles, in a nonconducting matrix during deposition causes an increase in the number of conductive paths which in turn, results in a very low base resistance. As discussed earlier, the formation of a conductive path is related to the percolation threshold of the material. The percolation threshold varies from material to material depending on factors, such as  
10   particle size, shape and composition. Alignment of the conductive region will cause percolation to occur at a much lower volume loading. Thus, sensors containing aligned conductive regions will give a larger signal when exposed to a vapor compared to a sensor without aligned regions. As the nonconductive region, such as an organic polymer, swells, disruption of the particle chains occurs and a lowering in the  
15   conductivity or an increase in the resistance occurs. As the polymer desorbs, the particles return to their minimum energy state that corresponds to particle alignment.

Non-sensor alignment of particles are known. For instance, U.S. Patent No. 4,177,228 issued to Prolss, entitled "Method of Production of a Micro-Porous Membrane for Filtration Plants," discloses the alignment of particles by various  
20   techniques. Likewise, U.S. Patent No. 5,742,223, issued to Simendding, entitled "Laminar Non-linear Device with Magnetically Aligned Particles," discloses composites with magnetically and electrically conductive particles. In addition, U.S. Patent No. 4,838,347, issued to Dentini, entitled "Thermal Conductor Assembly," discloses a polymer field with thermally conducting magnetically aligned particles. Furthermore,  
25   U.S. Patent No. 5,104,210, issued to Tokas, entitled "Light Control Films and Method of Making," discloses composites of magnetically alignable particles.

In certain aspects, the present invention relates to conductive regions capable of alignment including, but not limited to, conductive, semi-conductive, magnetic and photoresponsive particles embedded in a nonconductive region, such as an organic  
30   matrix. For instance, in one embodiment, particles suitable for use, while preferably spherical, are not limited by their shape and can even be in the form of flakes. Suitable particulate materials that are magnetic include, but are not limited to, metals such as, nickel, cobalt and iron and their magnetic alloys. Other suitable magnetic particles

include, but are not limited to, oxides and intermetallic compounds as are known in the art. Composite materials can also be used. These material include, but are not limited to, nickel coated with copper, or magnetically thermally conducting ceramics (*see*, U.S. Patent No. 4,838,347, incorporated herein by reference). Additional magnetic particles  
5 include, but are not limited to, alloys containing nickel, iron, cobalt and ferrites. Also conductive surface coatings can be used. Precious metal coatings include, but are not limited to, silver, gold and precious metal alloys (*see*, U.S. Patent Nos. 4,923,739 and 4,737,112 incorporated herein by reference).

10 In certain embodiments, the conductive region can be a substrate, such as a particle, coated with metal. Suitable substrates include, but are not limited to, glass, silicon, quartz, ceramic or combination thereof.

The present invention has advantages over current sensor technology. One advantage is the use of lower concentrations of particles, which leads to ease of dispersion. To a first approximation, the rate of particle sedimentation is proportional to  
15 the number of particles in the dispersion. Another advantage is the increased stability of the sensors of the present invention, especially when the polymer matrix is crosslinked (*i.e.*, the polymer molecules are interconnected forming a 3-dimensional network). A third advantage is an increase in the sensitivity of the sensors leading to lower limits of detection (*i.e.*, increased dynamic range). The latter advantage is due to the much higher  
20 signal-to-noise ratio given by the sensors having an aligned conductive region.

More particularly, the major advantage of this invention over the sensors of the prior art is that the signal-to-noise ratio is much higher. Because of the increase in the signal-to-noise ratio, the limit of detection increases (*i.e.*, a smaller concentration of analyte is capable of detection). In addition, the response time is faster. A faster  
25 response time is critical in applications such as quality control where the analyte may be on a conveyor belt with a very short time for detection. In general, sensors with greater response times are better than sensor with lower response times. Various sensor responses of the present invention include, but are not limited to, resistance, capacitance, inductance, impedance, and combinations thereof.

30 In certain aspects, the nonconductive region of the sensors comprise an organic material. In certain preferred aspects, the organic material is an organic polymer. Organic polymers suitable for use in the present invention include, but are not limited to, those set forth in Table 1.

TABLE 1

Major Class	Examples
Main-chain carbon polymers	poly(dienes), poly(alkenes), poly(acrylics), poly(methacrylics), poly(vinyl ethers), poly(vinyl thioethers), poly(vinyl alcohols), poly(vinyl ketones), poly(vinyl halides), poly(vinyl nitriles), poly(vinyl esters), poly(styrenes), poly(arylenes), etc.
Main-chain acyclic heteroatom polymers	poly(oxides), poly(carbonates), poly(esters), poly(anhydrides), poly(urethanes), poly(sulfonates), poly(siloxanes), poly(sulfides), poly(thioesters), poly(sulfones), poly(sulfonamides), poly(amides), poly(ureas), poly(phosphazenes), poly(silanes), poly(silazanes), etc.
Main-chain heterocyclic polymers	poly(furan tetracarboxylic acid diimides), poly(benzoxazoles), poly(oxadiazoles), poly(benzothiazinophenothiazines), poly(benzothiazoles), poly(pyrazinoquinoxalines), poly(pyromellitimides), poly(quinoxalines), poly(benzimidazoles), poly(oxindoles), poly(oxoisindolines), poly(dioxoisindolines), poly(triazines), poly(pyridazines), poly(piperazines), poly(pyridines), poly(piperidines), poly(triazoles), poly(pyrazoles), poly(pyrrolidines), poly(carboranes), poly(oxabicyclononanes), poly(dibenzofurans), poly(phthalides), poly(acetals), poly(anhydrides), carbohydrates, etc.

The sensors of the present invention can be fabricated by many techniques including, but not limited to, solution casting, suspension casting, matrix assisted pulsed laser evaporation (MAPLE), MAPLE-Direct Write (MAPLE-DW) (see, R. Andrew McGill, *et al.*, *IEEE Transactions on Ultrasonics, Ferroelectrics, and Frequency Control* 45:1370-1380 (1998), and mechanical mixing. In general, solution casting routes are advantageous because they provide homogeneous structures and are easy to process.



With solution casting routes, resistor elements can be easily fabricated by spin, spray or dip coating. Since all elements of the resistor must be soluble, solution casting routes can be somewhat limited in their applicability. Suspension casting still provides the possibility of spin, spray or dip coating, but more heterogeneous structures than with solution casting are expected. With mechanical mixing, there are no solubility restrictions since it involves only the physical mixing of the resistor components, but device fabrication is more difficult since spin, spray and dip coating are no longer possible. In certain embodiments, the resistor is deposited as a surface layer on a solid matrix that provides means for supporting the leads. Typically, the solid matrix is a chemically inert, nonconductive substrate, such as a glass or ceramic.

Sensor arrays of the present invention are particularly well-suited to scaled up production by being fabricated using integrated circuit (IC) design technologies. For example, the chemiresistors can easily be integrated onto the front end of a simple amplifier interfaced to an A/D converter to efficiently feed the data stream directly into a neural network software or hardware analysis section. Micro-fabrication techniques can integrate the chemiresistors directly onto a micro-chip that contains the circuitry for analogue signal conditioning/processing and then data analysis. This provides for the production of millions of incrementally different sensor elements in a single manufacturing step using ink-jet technology. Controlled compositional gradients in the chemiresistor elements of a sensor array can be induced in a method analogous to how a color ink-jet printer deposits and mixes multiple colors. However, in this case, rather than multiple colors, a plurality of different polymers in a solution which can be deposited are used. A sensor array of a million distinct elements only requires a 1 cm x 1 cm sized chip employing lithography at the 10  $\mu$ m feature level, which is within the capacity of conventional commercial processing and deposition methods. This technology permits the production of sensitive, small-sized, stand-alone chemical sensors.

The fabrication of the sensors of the present invention involves polarization processing of the conductive material. Suitable polarization processing includes, but is not limited to, magnetic field processing which involves exposure to magnetic fields, photolytic field processing which involves exposure to optical radiation, electric field processing which involves exposure to electric fields, and combinations thereof. In photolytic field processing, light sensitive material can be exposed to optical

radiation, such as visible, infrared, or ultraviolet light (*see*, U.S. Patent No. 4,737,112). All of the foregoing polarization processing techniques can have different axes direction and different strengths.

Preferred sensor arrays have a predetermined inter-sensor variation in the structure or composition of the nonconductive regions (*e.g.*, the nonconductive organic material). The variation can be quantitative and/or qualitative. For example, the concentration of the nonconductive organic material in the blend can be varied across sensors. Alternatively, a variety of different alignment techniques are possible within the sensor array. For example, the polarization processing techniques (*e.g.*, magnetic and electric fields) can vary across the array of sensors.

An electronic nose for detecting an analyte in a fluid is fabricated by electrically coupling the sensor leads of an array of compositionally different sensors to an electrical measuring device. The device measures changes in resistivity at each sensor of the array, preferably simultaneously and preferably over time. Frequently, the device includes signal processing means and is used in conjunction with a computer and data structure for comparing a given response profile to a structure-response profile database for qualitative and quantitative analysis.

As such, in another embodiment, the present invention, relates to a system for detecting an analyte in a fluid, comprising: a sensor array comprising first and second sensors wherein the first sensor comprises a region of aligned conducting material. Preferably, the first and second sensors are first and second chemically sensitive resistors, each chemically sensitive resistor comprising a plurality of alternating regions comprising a nonconductive region, such as a nonconductive organic material, and an aligned conductive region, such as an aligned conductive material compositionally different than the nonconductive region. Each resistor provides an electrical path through the alternating nonconducting region and the aligned conductive regions, a first response such as an electrical resistance, when contacted with a first fluid comprising an analyte at a first concentration and a second different response when contacted with a second fluid comprising the analyte at a second different concentration, the difference between the first response and the second response of the first sensor being different from the difference between the first response and the second response of the second sensor under the same conditions; an electrical measuring device electrically connected to the sensor array; and a computer comprising a resident algorithm; the electrical measuring device

detecting the first and said second responses in each of the sensors and the computer assembling the responses into a sensor array response profile.

Typically, such sensor arrays and electronic noses of the present invention comprise at least ten, usually at least 100, and often at least 1000 different sensors, though  
5 with mass deposition fabrication techniques described herein or otherwise known in the art, arrays of on the order of at least  $10^6$  sensors are readily produced.

In operation, preferably each resistor provides a first electrical resistance between its conductive leads when the resistor is contacted with a first fluid comprising an analyte at a first concentration, and a second electrical resistance between its  
10 conductive leads when the resistor is contacted with a second fluid comprising the same analyte at a second different concentration. The fluids can be liquid or gaseous in nature. The first and second fluids may reflect samples from two different environments, a change in the concentration of an analyte in a fluid sampled at two time points, a sample and a negative control, *etc.* The sensor array necessarily comprises sensors that respond  
15 differently to a change in an analyte concentration, *i.e.*, the difference between the first and second electrical resistance of one sensor is different from the difference between the first and second electrical resistance of another sensor. In addition, the sensor array can comprise redundant sensors that can be advantageous for maximizing the signal and thus reducing the noise in the signal.

20 In a preferred embodiment, the temporal response of each sensor (resistance as a function of time) is recorded. The temporal response of each sensor may be normalized to a maximum percent increase and percent decrease in resistance which produces a response pattern associated with the exposure of the analyte. By iterative profiling of known analyses, a structure-function database correlating analyses and  
25 response profiles is generated. Unknown analyte can then be characterized or identified using response pattern comparison and recognition algorithms. Accordingly, analyte detection systems comprising sensor arrays, an electrical measuring device for detecting resistance across each chemiresistor, a computer, a data structure of sensor array response profiles, and a comparison algorithm are provided. In another embodiment, the electrical  
30 measuring device is an integrated circuit comprising neural network-based hardware and a digital-analog converter (DAC) multiplexed to each sensor, or a plurality of DACs, each connected to different sensor(s).

A wide variety of analytes and fluids may be analyzed by the disclosed sensors, arrays and noses so long as the subject analyte is capable of generating a differential response across a plurality of sensors of the array. Analyte applications include broad ranges of chemical classes including, but not limited to, organics such as alkanes, alkenes, alkynes, dienes, alicyclic hydrocarbons, arenes, heterocyclics, alcohols, ethers, ketones, aldehydes, carbonyls, carbanions, polynuclear aromatics and derivatives of such organics, *e.g.*, halide derivatives, *etc.*, microorganism off-gases, fungi, bacteria, microbes, viruses, metabolites, biomolecules such as sugars, isoprenes and isoprenoids, fatty acids and derivatives, *etc.*

Accordingly, commercial applications of the sensors, arrays and noses include environmental toxicology and remediation, biomedicine, materials quality control, food and agricultural products monitoring. Further applications include, but are not limited to: heavy industrial manufacturing (automotive, aircraft, *etc.*), such as ambient air monitoring, worker protection, emissions control, and product quality testing; oil/gas petrochemical applications, such as combustible gas detection, H<sub>2</sub>S monitoring, and hazardous leak detection and identification; emergency response and law enforcement applications, such as illegal substance detection and identification, arson investigation, hazardous spill identification, enclosed space surveying, and explosives detection; utility and power applications, such as emissions monitoring and transformer fault detection; food/beverage/agriculture applications, such as freshness detection, fruit ripening control, fermentation process monitoring and control, flavor composition and identification, product quality and identification, and refrigerant and fumigant detection; cosmetic/perfume applications, such as fragrance formulation, product quality testing, and patent protection fingerprinting; chemical/plastics/pharmaceuticals applications, such as fugitive emission identification, leak detection, solvent recovery effectiveness, perimeter monitoring, and product quality testing; hazardous waste site applications, such as fugitive emission detection and identification, leak detection and identification, and perimeter monitoring; transportation applications, such as hazardous spill monitoring, refueling operations, shipping container inspection, and diesel/gasoline/aviation fuel identification; building/residential applications, such as natural gas detection, formaldehyde detection, smoke detection, automatic ventilation control (cooking, smoking, *etc.*), and air intake monitoring; hospital/medical applications, such as

anesthesia and sterilization gas detection, infectious disease detection, breath, wound and body fluids analysis, and telesurgery.

In yet another aspect, the present invention relates to a method for detecting the presence of an analyte in a fluid comprising: providing a sensor array comprising first and second sensors, wherein the first sensor comprises a region of aligned conductive material; and contacting the sensor array with the analyte to produce a response thereby detecting the presence of the analyte. Preferably, the first and second sensors are first and second chemically sensitive resistors each comprising a plurality of alternating nonconductive regions, such as nonconductive organic material, and aligned conductive regions, such as an aligned conductive material compositionally different than the nonconductive region, each resistor providing an electrical path through the nonconducting region and aligned conductive region, a first response such as an electrical resistance, when contacted with a first fluid comprising an analyte at a first concentration and a second different response when contacted with a second fluid comprising the analyte at a second different concentration.

The general method for using the disclosed sensor arrays and electronic noses for detecting the presence of an analyte in a fluid preferably involves resistively sensing the presence of an analyte in a fluid with a chemical sensor comprising first and second conductive leads electrically coupled to and separated by a chemically sensitive resistor as described above by measuring a first resistance between the conductive leads when the resistor is contacted with a first fluid comprising an analyte at a first concentration and a second different resistance when the resistor is contacted with a second fluid comprising the analyte at a second different concentration.

In certain embodiments, the methods and systems of the present invention can be used for monitoring medical conditions and disease processes. For instance, WO 98/29563, published July 9, 1998, and incorporated herein by reference, discloses a method for monitoring conditions in a patient wherein a sample is obtained from a patient over a period of time. The samples are then flowed over a gas sensor and a response is measured. Thereafter, the response is correlated with known responses for known conditions. The conditions include, but are not limited to, the progression and or regression of a disease state, bacterial infections, viral, fungal or parasitic infections, the effectiveness of a course of treatment and the progress of a healing process.

In another embodiment, the methods and systems of the present invention can be used for monitoring medical conditions in a respiring subject. For instance, WO 98/39470, published September 11, 1998, and incorporated herein by reference, discloses a method for detecting the occurrence of a condition in a respiring subject. The method  
5 comprises introducing emitted respiratory gases to a gas sensing device, detecting certain species present in the gas and correlating the presence of the species with certain conditions. A wide variety of conditions can be ascertained using this aspect of the present invention. These conditions include, but are not limited to, halitosis, ketosis, yeast infections, gastrointestinal infections, diabetes, alcohol, phenylketonuria,  
10 pneumonia, and lung infections. Those of skill in the art will know of other conditions and diseases amenable to the methods and systems of the present invention.

In certain aspects, the sensor arrays, systems and methods of the present invention comprise: first and second sensors wherein the first sensor comprises a region of aligned conducting material. The second sensor can also comprise a region of aligned  
15 conductive material. However, in certain other embodiments, the second sensor is a different sensor type. Suitable sensor types include, but are not limited to, a surface acoustic wave (SAW) sensor; a quartz microbalance sensor; a conductive composite; a metal oxide gas sensor, an organic gas sensor; an infrared sensor; a sintered metal oxide sensor; a phthalocyanine sensor; an electrochemical cell; a conducting polymer sensor; a  
20 catalytic gas sensor; an organic semiconducting gas sensor; a solid electrolyte gas sensor; a temperature sensor; a humidity sensor; fiber optic micromirrors; dye impregnated polymeric coatings on optical fibers and a Langmuir-Blodgett film sensor. Those of skill in the art will know of other sensors suitable for use in the present invention.

In certain aspects, the sensors of the present invention comprise a chiral  
25 center. For instance, European Patent Application No. 0 794 428, published September 10, 1997, describes sensors capable of distinguishing between enantiomers. The sensor comprise a pair of spaced apart contacts and a conducting polymer material spanning the gap. The polymer has chiral sites in the polymer material formed by incorporating optically active counter ions such as camphor sulfonic acid.

30 Moreover, WO 99/40423, published August 12, 1999, discloses sensor arrays of that are capable of distinguishing or differentiating between chiral compounds. That publication relates to a device for detecting the presence or absence of an analyte in a fluid, the device comprises a sensor, the sensor comprising a chiral region. The sensor

comprises a conductive region and a nonconductive region, wherein at least one of the conductive and nonconductive regions is chiral, and wherein the analyte generates a differential response across the sensor.

In certain other embodiments, the sensor arrays of the present invention  
5 comprise sensors disclosed in WO 99/00663, published January 7, 1999. As taught therein, a combinatorial approach for preparing arrays of chemically sensitive polymer-based sensors are capable of detecting the presence of a chemical analyte in a fluid contact therewith. The described methods and devices comprise combining varying ratios of at least first and second organic materials which, when combined, form a polymer or  
10 polymer blend that is capable of absorbing a chemical analyte, thereby providing a detectable response. The detectable response of the sensors prepared by this method is not linearly related to the mole fraction of at least one of the polymer-based components of the sensor.

The following examples are offered by way of illustration and not by way  
15 of limitation.

## EXAMPLES

### Example 1

This Example illustrates the difference in percolation threshold in non-  
20 aligned sensors versus aligned sensors.

The percolation threshold is defined as the particle volume fraction at which the conductivity of the resistor increases rapidly *i.e.*, an infinite number of conductive paths are formed and the lattice essentially transforms from an insulator to a conductor. Figure 1 illustrates a typical resistance versus volume loading for a non-  
25 aligned composite sensor, where the percolation threshold occurs at about 20 volume percent filler. Figure 2 shows a graph of resistance versus volume loading for a composite sensor where the particles have been aligned. The percolation threshold occurs at about 5 volume percent filler.

**Example 2**

This Example illustrates a sensor array that was fabricated by depositing Black Pearl 2000 (40 wt %) dispersed in 1,2-polybutadiene in the presence of an electric field.

5           The conductive particles respond to the field by migrating to minimum energy states, which in this case corresponds to chain-like structures aligned parallel to the electric field. As the solvent evaporates the chains are locked in place. Figure 3 illustrates the particle alignment after using 48 volts across the sensor electrodes during the deposition process.

10           All publications, patents and patent applications mentioned in this specification are herein incorporated by reference into the specification in their entirety for all purposes. Although the invention has been described with reference to preferred embodiments and examples thereof, the scope of the present invention is not limited only to those described embodiments. As will be apparent to persons skilled in the art,  
15       modifications and adaptations to the above-described invention can be made without departing from the spirit and scope of the invention, which is defined and circumscribed by the appended claims.



**WHAT IS CLAIMED IS:**

1                   1.       A sensor array for detecting an analyte in a fluid, said sensor array  
2 comprising: first and second sensors wherein said first sensor comprises a region of  
3 aligned conductive material; and wherein said sensor array is electrically connected to an  
4 electrical measuring apparatus.

1                   2.       The sensor array for detecting an analyte in a fluid in accordance  
2 with claim 1, wherein said first and said second sensors are first and second chemically  
3 sensitive resistors, each of the chemically sensitive resistors comprising: a plurality of  
4 alternating regions comprising a nonconductive region and an aligned conductive region  
5 that is compositionally different than the nonconductive region, wherein each resistor  
6 provides an electrical path through said nonconductive region and the aligned conductive  
7 region; a first electrical resistance when contacted with a first fluid comprising an analyte  
8 at a first concentration; and a second electrical resistance when contacted with a second  
9 fluid comprising said analyte at a second different concentration.

1                   3.       The sensor array for detecting an analyte in a fluid in accordance  
2 with claim 1, wherein said conductive region is aligned by exposure to a member selected  
3 from the group consisting of an electric field, a thermal field, a magnetic field, an  
4 electromagnetic field, a photoelectric field, a light field, a mechanical field, and  
5 combinations thereof.

1                   4.       The sensor array for detecting an analyte in a fluid in accordance  
2 with claim 3, wherein said conductive region is electrically aligned.

1                   5.       The sensor array for detecting an analyte in a fluid in accordance  
2 with claim 3, wherein said conductive region is magnetically aligned.

1                   6.       The sensor array for detecting an analyte in a fluid in accordance  
2 with claim 3, wherein said conductive region is photolytically aligned.

1                   7.       The sensor array for detecting an analyte in a fluid in accordance  
2 with claim 1, wherein said aligned conductive material is a member selected from the

3 group consisting of metal, magnetic alloys, ceramics, oxides, intermetallic compounds,  
4 carbon black, nanoparticles and composite materials.

1                   8.       The sensor array for detecting an analyte in a fluid in accordance  
2 with claim 7, wherein said conductive material comprises carbon black.

1                   9.       The sensor array for detecting an analyte in a fluid in accordance  
2 with claim 7, wherein said conductive material comprises a nanoparticle.

1                   10.      The sensor array for detecting an analyte in a fluid in accordance  
2 with claim 7, wherein said conductive material comprises a metal.

1                   11.      The sensor array for detecting an analyte in a fluid in accordance  
2 with claim 10, wherein said metal is a member selected from the group consisting of  
3 nickel, cobalt, iron, a ferrite and their magnetic alloys.

1                   12.      The sensor array for detecting an analyte in a fluid in accordance  
2 with claim 10, wherein said metal is a coating of a substrate, said substrate is a member  
3 selected from group consisting of glass, silicon, quartz, ceramic or combination thereof.

1                   13.      The sensor array for detecting an analyte in a fluid in accordance  
2 with claim 10, wherein said metal is a member selected from the group consisting of a  
3 precious metal coating and precious metal alloys.

1                   14.      The sensor array for detecting an analyte in a fluid in accordance  
2 with claim 13, wherein said precious metal coating is a member selected from the group  
3 consisting of silver, gold and platinum.

1                   15.      The sensor array for detecting an analyte in a fluid in accordance  
2 with claim 7, wherein said conductive region is an oxide.

1                   16.      The sensor array for detecting an analyte in a fluid in accordance  
2 with claim 15, wherein said conductive region is a member selected from the group  
3 consisting of  $\text{In}_2\text{O}_3$ ,  $\text{SnO}_2$ ,  $\text{Na}_x\text{Pt}_3\text{O}_4$ ,  $\text{TiO}_2$  and  $\text{BaTiO}_3$ .

1                   17.     The sensor array for detecting an analyte in a fluid in accordance  
2 with claim 1, wherein said aligned region is a material selected from the group consisting  
3 of copper phthalocyanine and phenothiazine.

1                   18.     A system for detecting an analyte in a fluid, said system  
2 comprising:  
3                   a sensor array comprising first and second sensors wherein said first sensor  
4 comprises a region of aligned conductive material which provides a response in the  
5 presence of said analyte;  
6                   an electrical measuring device electrically connected to the sensor array;  
7                   and a computer comprising a resident algorithm; the electrical measuring  
8 device detecting the response and the computer assembling the response into a sensor  
9 array response profile.

1                   19.     The system for detecting an analyte in a fluid in accordance with  
2 claim 18, wherein said first and said second sensors are first and second chemically  
3 sensitive resistors, each chemically sensitive resistor comprising a plurality of alternating  
4 regions comprising a nonconductive region and an aligned conductive region that is  
5 compositionally different than said nonconductive region wherein,  
6                   each resistor provides an electrical path through said nonconductive region  
7 and said aligned conductive region, a first electrical resistance when contacted with a first  
8 fluid comprising an analyte at a first concentration and a second different electrical  
9 resistance when contacted with a second fluid comprising said analyte at a second  
10 different concentration wherein,  
11                   the difference between said first electrical resistance and said second  
12 electrical resistance of said first chemically sensitive resistor being different from the  
13 difference between said first electrical resistance and said second electrical resistance of  
14 said second chemically sensitive resistor under the same conditions; and  
15                   the electrical measuring device detecting the first and said second  
16 electrical resistances in each of said chemically sensitive resistors and the computer  
17 assembling the resistances into a sensor array response profile.

1                   20.     The system for detecting an analyte in a fluid in accordance with  
2 claim 18, wherein said conductive region is aligned by exposure to a member selected

3 from the group consisting of an electric field, a thermal field, a magnetic field, an  
4 electromagnetic field, a photoelectric field, a light field or combinations thereof.

1           21.     The system for detecting an analyte in a fluid in accordance with  
2 claim 20, wherein said conductive region is electrically aligned.

1           22.     The system for detecting an analyte in a fluid in accordance with  
2 claim 20, wherein said conductive region is magnetically aligned.

1           23.     The system array for detecting an analyte in a fluid in accordance  
2 with claim 20, wherein said conductive region is photolytically aligned.

1           24.     A method for detecting the presence of an analyte in a fluid, said  
2 method comprising:  
3                 providing a sensor array comprising first and second sensors, wherein said  
4 first sensor comprises a region of aligned conductive material; and  
5                 contacting said sensor array with said analyte to produce a response  
6 thereby detecting the presence of the analyte.

1           25.     The method for detecting an analyte in a fluid in accordance with  
2 claim 24, wherein said first and said second sensors are first and second chemically  
3 sensitive resistors each comprising a plurality of alternating regions comprising a  
4 nonconductive region, and an aligned conductive region that is compositionally different  
5 than the nonconductive material, and wherein each resistor provides an electrical path  
6 through said nonconducting regions and aligned conductive regions, a first electrical  
7 resistance when contacted with a first fluid comprising an analyte at a first concentration  
8 and a second different electrical resistance when contacted with a second fluid comprising  
9 said analyte at a second different concentration.

1           26.     The method for detecting an analyte in a fluid in accordance with  
2 claim 24, wherein said conductive region is electrically aligned.

1           27.     The method for detecting an analyte in a fluid in accordance with  
2 claim 24, wherein said conductive region is magnetically aligned.

- 1                   28.    The method for detecting an analyte in a fluid in accordance with  
2   claim 24, wherein said conductive region is photolytically or mechanically aligned.

Fig. 1

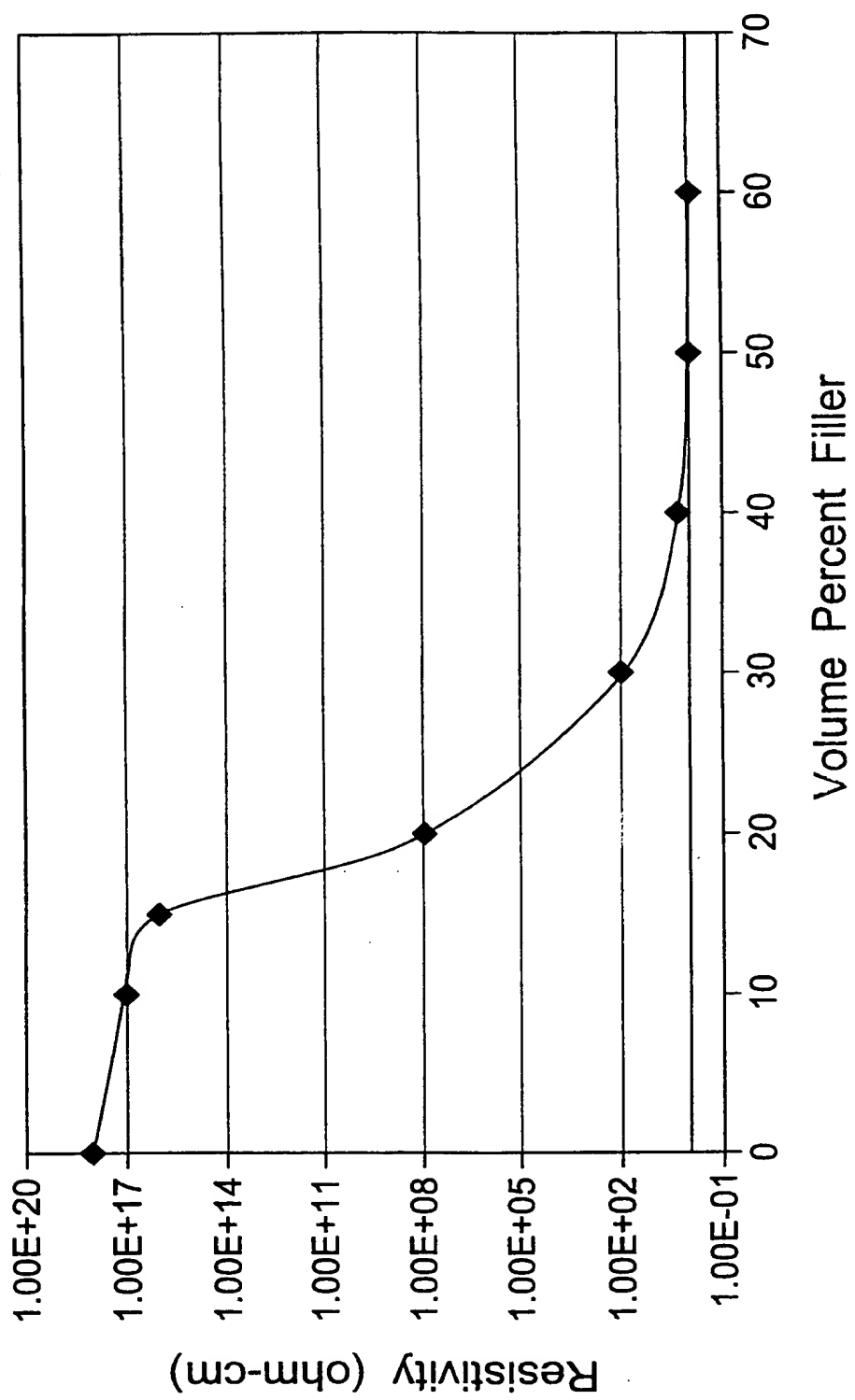


Fig. 2

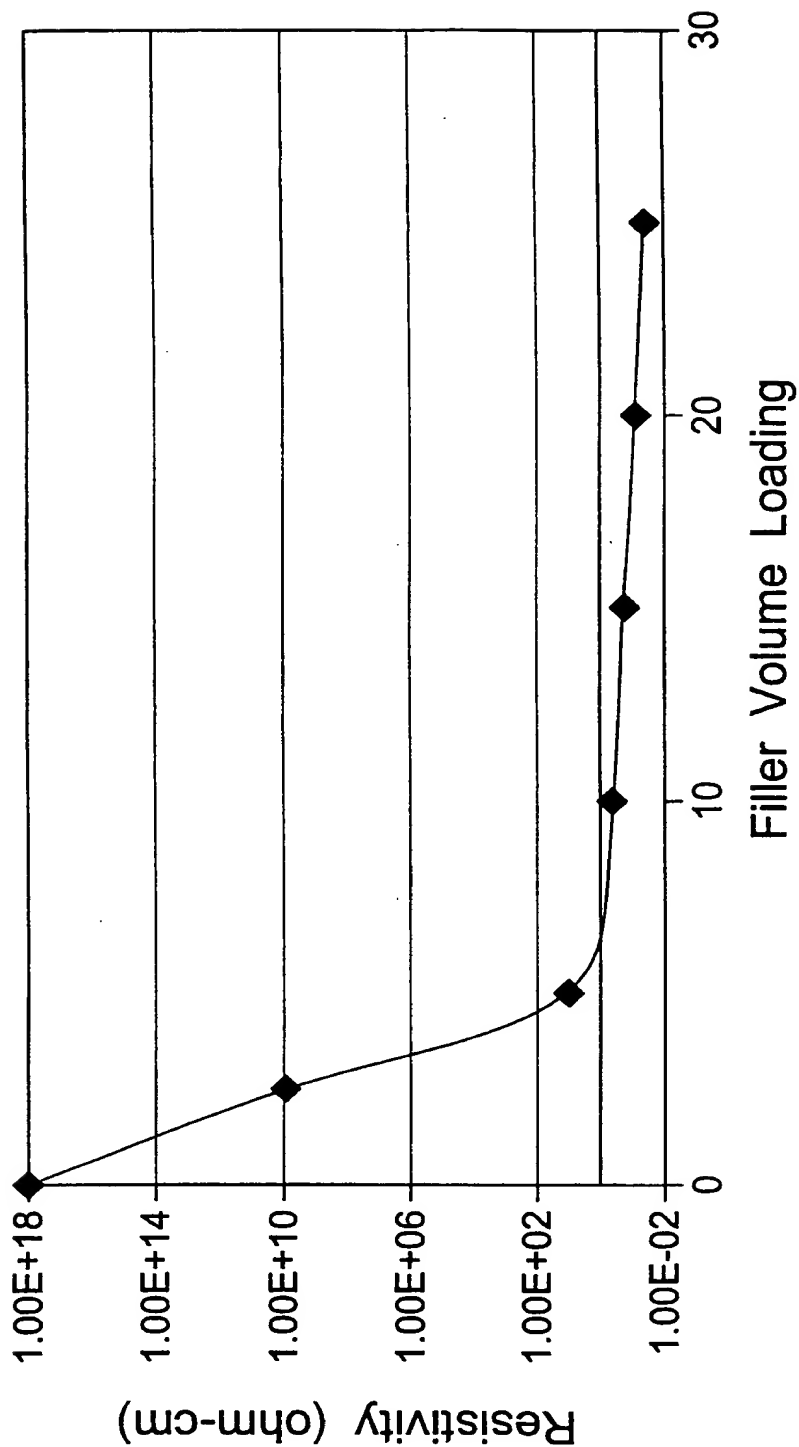
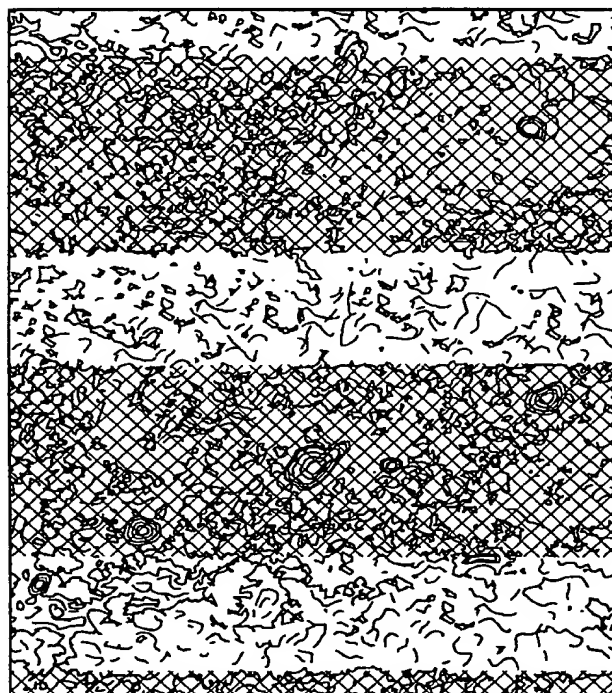
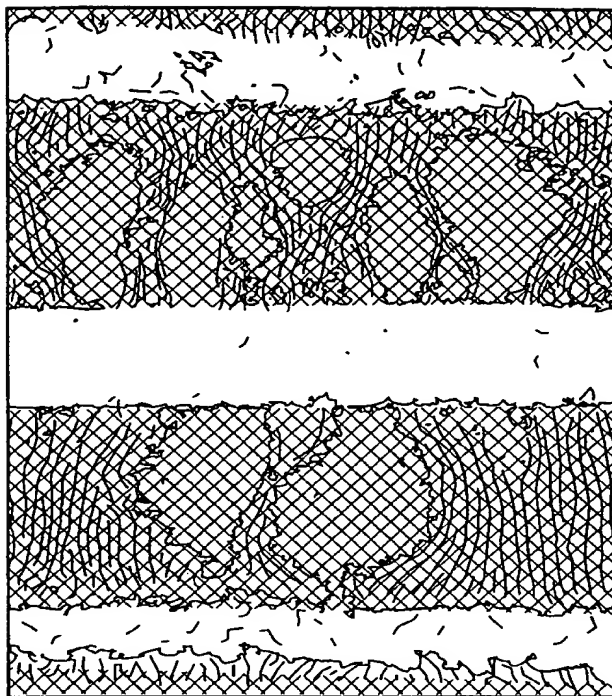


Fig. 3





## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US99/28282

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(7) : Please See Extra Sheet.

US CL : Please See Extra Sheet.

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

U.S. : Please See Extra Sheet.

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

None

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Please See Extra Sheet.

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5,742,223 A (SIMENDINGER, III et al.) 21 April 1998 (21-04-1998), Col. 2 line 13 - Col. 6 line 59, Col. 7 line 30 - Col. 8 line 21, and Fig. 1.	1-3, 5, 7-15, 18-22, 24-25, 27
Y	US 5,571,401 A (LEWIS et al.) 05 November 1996 (05-11-1996), Col. 2 lines 1-38, Col. 3 line 39 - Col. 8 line 17, Col. 13 line 21 - Col. 15 line 7, and Figs. 1A, 1B, 5, 8 & 9.	1-3, 5, 7-15, 18-20, 22, 24-25, 27
Y	US 4,737,112 A (JIN et al.) 12 April 1988 (12-04-1988), Col. 1 lines 21-60, Col. 3 lines 3-68, Col. 4 lines 42-49 and Fig. 1.	1-3, 5, 7-15, 18-20, 22, 24-25, 27-28
A	US 5,942,674 A (LOGOTHETIS et al.) 24 August 1999 (24.08.99), see entire document.	1-2, 10-13, 15, 18-19, 24-25

☒ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E" earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O" document referring to an oral disclosure, use, exhibition or other means		
"P" document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search

09 FEBRUARY 2000

Date of mailing of the international search report

21 APR 2000

Name and mailing address of the ISA/US  
Commissioner of Patents and Trademarks  
Box PCT  
Washington, D.C. 20231

Facsimile No. (703) 305-3230

Authorized officer

DAVID JOHN WIGGINS

Telephone No. (703) 305-4884

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US99/28282

## C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 4,453,126 A (VOLGYESI) 05 June 1984 (05-06-1984), see entire document.	1-2, 18-19, 23-26
A	US 4,198,851 A (JANATA) 22 April 1980 (22-04-1980), see entire document.	1, 2, 7, 9-10, 12, 15, 17-19, 24- 25, 28
A	US 4,923,739 A (JIN et al.) 08 May 1990 (08-05-1990), see entire document.	1-3, 4, 5, 6, 7, 10-11, 13-15, 18-20, 22, 24-25, 27
A	US 4,644,101 A (JIN et al.) 17 February 1987 (17-02-1987), see entire document.	1-3, 5, 7, 10-14, 18-20, 22, 24-25, 27
A	US 5,512,882 A (STETTER et al.) 30 April 1996 (30-04-1996), see entire document.	1-2, 24-25

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US99/28282

## A. CLASSIFICATION OF SUBJECT MATTER:

IPC (7):

G01N 27/26, 27/12, 27/22, 31/06; G08B 17/10; G01R 27/26; H01C 07/10; H01R 09/09

## A. CLASSIFICATION OF SUBJECT MATTER:

US CL :

073/31.05, 23.32; 324/71.1; 340/632; 338/21; 422/098, 090, 83, 68.1, 82.02; 205/787, 775, 782.5; 204/418, 415, 406; 436/150

## B. FIELDS SEARCHED

Minimum documentation searched

Classification System: U.S.

073/31.05, 23. 32, 23.2, 31.06, 28.01; 324/71.1; 340/632; 338/21; 422/098, 090, 83, 68.1, 82.02; 205/787, 775, 782.5; 204/418, 415, 406; 436/150; 439/066; 428/900, 221; 439/065

## B. FIELDS SEARCHED

Electronic data bases consulted (Name of data base and where practicable terms used):

USPTO APS WEST/EAST computer database of Derwent & US Patents Search Terms: aligned or oriented or parallel or ordered; electrical, dipole, flux, field, dielectric, susceptibility, permeability or magnetic; electrical current, discharge, avalanche, resistance or impedance; path or route; array, plurality, multitude, group or family; sensors, detectors, probes, analyzers or chemFET's; conducting or nonconducting or insulating or semiconducting; bands, stripes, areas, spots, patches, regions or zones; chemical or catalyst; reactive or sensitive; resistor or transistor; analyte, component, particle, constituent or species; solution, fluid, vapor, suspension or gas.